The actual exercise duration, ETT variables, other clinical history or medical regimens were not predictive. Free of cardiac events were 66% (CI 53–82) at 5 yrs and 47% (CI 33–68) at 10 yrs. The survival rate was 95% (CI 0.89–1.0) at 5 yrs and 85% (CI 0.71–1.0) at 10 yrs. *Conclusions: 1.* SED alone does not constitute an adverse outcome. *2.* In second opinion CAD patients managed with medical therapy and a short exercise duration, mortality is not predicted by ETT variables, but by type of angina and medical regimen.

952-110 Dipyridamole Induced ST-segment Depression Predicts Ischemia in Patients With Left Ventricular Hypertrophy by ECG

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ST-segment depression (STdpr) in the presence of LVH by ECG is an unreliable marker of ischemia during exercise stress testing. Dipyridamole (DP) induced STdpr is a highly specific marker of ischemia, however its significance is unknown in patients (pts) with LVH by ECG. We studied 484 consecutive pts undergoing DP perfusion imaging (0.57 mg/kg over 4 min with sestamibi injection at 8 min) for development of ≥ 1 mm horizontal or downsloping STdpr. An additional 1 mm STdpr was required if baseline STdpr was present. LVH was defined by standard ECG criteria. Ischemia was defined as any new perfusion defect compared to the resting scan. Pts with LBBB or ventricular paced rhythm (n = 31) were excluded. Four groups were identified: LVH with STdpr, LVH without STdpr, STdpr without LVH, no STdpr no LVH. Antianginal and digoxin use was similar among groups. STdpr occurred in 22/78 (28%) pts with LVH versus 35/375 (9.3%) pts without LVH ($p < 0.001$). Ischemia occurred in 15/22 (68%) LVH pts with STdpr versus 14/56 (25%) LVH pts without STdpr ($p = 0.002$). Ischemia frequency was similar in STdpr pts regardless of LVH by ECG ($p = 0.28$). DP infusion increased heart rate and rate-pressure product (RPP) and decreased blood pressure in each group. LVH pts with STdpr had higher resting and peak heart rates and RPP as compared to LVH pts without STdpr (all $p < 0.04$). No significant difference in resting and peak heart rate and RPP was present among STdpr pts with or without LVH. Chest pain occured with higher frequency in LVH pts with STdpr vs without STdpr (11/22 vs 12/56; $p < 0.02$) but with similar frequency compared to STdpr pts without LVH.

Conclusions: (1) DP induced STdpr is more frequent in pts with vs without LVH by ECG. (2) The frequency of ischemia and hemodynamic effects induced by DP are similar in STdpr pts independent of LVH by ECG. (3) DP induced STdpr in pts with LVH by ECG is predictive of ischemia.

952-111 Mechanism of Preserved Exercise Capacity in Patients With Reduced Left Ventricular Function

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To elucidate the mechanism of preserved exercise capacity in patients with reduced left ventricular (LV) function, 71 patients with myocardial infarction underwent a symptom-limited invasive cardiopulmonary exercise test with a cycle ergometer in a supine position. Patients were divided into two groups according to LV ejection fraction (EF) at rest; Group A (n = 20): EF > 40% (avr. 56 ± 6%), Group B (n = 51): EF ≤ 40% (avr. 31 ± 7%). Cardiac output and LV pressure were measured with a Swan-Ganz catheter and a tipped catheter, respectively, at rest and during exercise. LV stiffness index was calculated as (left ventricular end-diastolic pressure − minimum pressure)/stroke volume index (SI).

	CI	SI	HR	a-vDO2	VO2	Stiffness
A Rest	4.1 ± 0.8	56 ± 9	75 ± 11	3.2 ± 0.8	3.6 ± 0.8	0.2 ± 0.1
Peak	8.1 ± 1.9	65 ± 12	125 ± 20	8.1 ± 1.8	16.5 ± 4.9	0.3 ± 0.1
B Rest	3.7 ± 0.8*	48 ± 8#	76 ± 10	3.7 ± 0.9#	3.5 ± 0.7	0.3 ± 0.1#
Peak	6.7 ± 1.5#	53 ± 10#	128 ± 18	9.0 ± 1.5*	16.3 ± 4.4	0.4 ± 0.1#

CI: cardiac index (l/min/m^2), SI (ml/m^2), HR: heart rate (bpm), a-vDO2: arteriovenous O2 difference (ml/dl), VO2: O2 uptake (ml/min/kg), Stiffness: LV stiffness index, Peak: peak exercise. *$p < 0.05$, #$p < 0.01$ vs. Group A.

Patients with reduced EF showed not only reduced CI and SI but also impaired diastolic function both at rest and during exercise. However, peak VO2 was comparable to that of the patients with higher EF, because a-vDO2 fully compensated the reduced CI. Conclusion: In patients with reduced LVEF, exercise capacity is preserved by a compensatory increase in a-vDO2. HR and LV diastolic function are not likely to play a compensatory role in this setting.

952-112 Maximal Exercise Testing Early After Myocardial Infarction — Better to Predict Cardiac Events?

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The aim of this prospective study was to evaluate if predischarge maximal exercise treadmill testing (ETT) after myocardial infarction (MI) is superior to the classic low level (HR < 70% of age predicted) ETT, for risk stratification.

We studied a group of 124 consecutive patients (P), 111 men and 13 women, mean age 56.1 ± 9.7 years, admitted with MI (52 inferior, 48 anterior, 24 non-Q) who performed a predischarge (10.4 ± 2.3 days) symptom limited ETT, without anti-ischemic medication, using a modified Bruce protocol. There was no major complications. We have registered in all patients some variables (exercise duration, symptoms, HR, systolic BP, double product, ST segment depression and arrhythmias) at HR = 70% and at peak exercise. Only 13 P had not achieved a HR > 70% of predicted. 23 P had positive (ST-segment depression with or without chest pain) ETT at HR < 70% and 18 additional P had positive ETT at HR > 70%. In the follow-up (mean 20.7 ± 5.2 months) 51 P suffered cardiac events (recurrent angina, reinfarction, cardiac death, PTCA, CABG). Of these 51 P only 18 had a positive test at low level but 32 P had positive test at peak exercise. 33 P with negative ETT at HR < 70% had suffered events versus only 19 P with negative maximal ETT. 14 of the 18 P (78%) with positive ETT only after HR > 70% (P with negative low level ETT) had cardiac events in the follow-up.

Predischarge ETT for detection cardiacs events in the follow-up:

	HR < 70%	Maximal
Sensitivity	0.35	0.63
Specificity	0.93	0.88
Predictive Value (+)	0.78	0.78
Predictive Value (−)	0.67	0.77

Conclusion: Predischarge maximal ETT appears to be safe and better than low level ETT for risk stratification after MI.

952-113 Relationship Between Resting Blood Pressure and Perception of Angina Pectoris During Exercise

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Previous studies in animals and humans have shown decreased pain perception in hypertensives. To test the hypothesis that resting blood pressure influences anginal pain perception during exercise, we reviewed 4723 exercise treadmill test results performed at UNC Hospitals during 1990–1994. All tests were interpreted by one cardiologist. 1144 tests were positive, defined as 1 mm horizontal or downsloping ST segment depression at 0.08 seconds after the J-point. Patients with conditions that affect anginal perception (diabetes mellitus, post CABG), exercise protocol other than Bruce, who were taking antianginal medication or digoxin were excluded. Patients with resting ECG abnormalities (LVH, LBBB, WPW), ECG changes with posture or hyperventilation were also excluded. Two hundred thirty five patients with positive tests remained after exclusion. Hemodynamic data were obtained at rest and during exercise (2 minutes into each stage). Angina was reported in 65 patients. Compared to patients with angina, patients without angina had a higher resting systolic (135 ± 1.6 vs 128 ± 2.2 mmHg, $p = 0.02$) and diastolic (83 ± 0.8 vs 80 ± 1.3 mmHg, $p = 0.04$) blood pressure without any differences in resting heart rate (79 ± 0.9 vs 78 ± 1.8bpm, p = ns). Time to onset of 1 mm ST depression and double product at 1 mm ST depression were the same for both groups. Fourteen out of 74 patients (19%) with resting SBP < 140 mmHg had angina during exercise whereas 51 out of 161 (32%) patients with resting SBP ≤ 140 mmHg had angina ($p = 0.04$). In conclusion: patients with higher resting blood pressure have less frequent angina during exercise. Thus resting blood pressure appears to be related to pain perception in patients with CAD.

952-114 Prediction of Maximal Oxygen Consumption by Six Minute Walk Testing in Patients With Congestive Heart Failure

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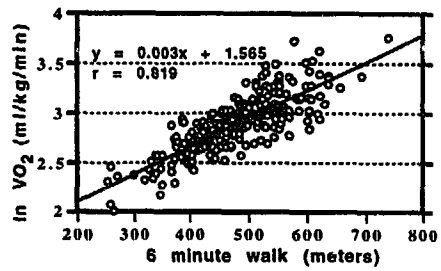
Maximal oxygen consumption (VO_2max) is widely used for risk stratification in CHF but is expensive and not widely available. The 6 minute walk test (6MW) provides an inexpensive and readily available measure of submaximal exercise capacity, and may be closely correlated to VO_2max. Therefore, we measured 6MW and VO_2max during treadmill exercise on CHF patients referred for functional assessment; data on 237 pts (190 men, 47 women; age 50.2 ± 11.4 years) who achieved R values ≥ 1.1 were included in this

analysis. Linear regression models were developed to predict ln(VO_2max) from 6MW with and without BSA, age, and sex.



Inclusion of BSA and age significantly improved the model (ln[VO_2max] *in ml/min* = 4.569 + 0.0026 (6MW) + 0.838 BSA – 0.0036 Age; r = 0.902). In conclusion, use of this regression model may, if validated, allow accurate prediction of VO_2 max from 6MW.

952-115 Arachidonic Acid-Induced Dilation of Epicardial Coronary Artery Is Maintained in Awake Dogs With Chronic Exercise Training Plus Rapid Cardiac Pacing

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Previous studies has shown that arachidonic acid(AA)-induced dilation of epicardial coronary artery (CA) is attenuated but PGI_2-induced dilation of CA is preserved in heart failure (CHF), suggesting that the attenuated response of AA is due to defective endothelial conversion of AA to prostacyclins. Since exercise training (EX) normalizes some aspects of endothelial function, the objective of this study was to determine whether EX improves AA-induced dilation of CA during development of CHF. Dogs(n = 6) were chronically instrumented for measurements of left ventricular and aortic pressure, coronary blood flow and diameter of CA and for chronic cardiac pacing. Dogs were cardiac paced for 4 wks and treadmill EX (4.4 ± 0.36 km/hour) was performed on a treadmill 2 hours/day throughout this 4 wks. Changes in CA diameter induced by AA were examined before (*Control*) and after this 4 wk period (*Pacing plus exercise*). The results are as follows:

	Baseline	Response	Δ	% Δ
Control				
AA 250 μg/kg	3.50 ± 0.26	3.63 ± 0.25	0.14 ± 0.03*	4.15 ± 1.10*
AA 500 μg/kg	3.50 ± 0.26	3.68 ± 0.26	0.18 ± 0.05*	5.23 ± 1.57*
After 4 wk pacing plus exercise				
AA 250 μg/kg	3.81 ± 0.21	3.93 ± 0.20	0.13 ± 0.02*	3.47 ± 0.74*
AA 500 μg/kg	3.79 ± 0.22	3.96 ± 0.22	0.17 ± 0.02*	4.52 ± 0.76*

values are CA diameter in mm. *p < 0.05 from baseline

This contrasts with previous results showing that the response of CA diameter to AA is eliminated in dogs with the same pacing regimen but without exercise. Thus, EX training protected endothelium/prostaglandin-mediated dilation of CA during development of CHF. This may indicate that the conversion of AA to prostacyclins was normalized by EX.

953 Basic Coronary Vascular Physiology – Miscellaneous

Tuesday, March 26, 1996, 9:00 a.m.–11:00 a.m.
Orange County Convention Center, Hall E
Presentation Hour: 9:00 a.m.–10:00 a.m.

953-89 Natriuretic Peptides Inhibit Endothelin-1 and Angiotensin-II Mediated Human Coronary Smooth Muscle Cell Proliferation

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Atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP) are a family of structurally related peptides that participate in the integrated control of renal and cardiovascular function via activation of particulate guanylyl cyclase and generation of cGMP. While an antimitogenic action for the natriuretic peptides have been investigated in non-human mammalian cells, the antiproliferative action of the natriuretic peptides in human coronary vascular smooth muscle cells (HCVSMC) proliferation remain undefined. Therefore, the current study was designed to investigate the inhibitory function of ANP, BNP and CNP upon endothelin-1 (ET-1) and angiotensin II (AII) mediated HCVSMC proliferation. Cultured HCSMC were stimulated by ET-1 (10^{-7} M) and AII (10^{-7} M) with and without ANP,.BNP and CNP (10^{-7} M each) and thymidine incorporation determined. These studies were repeated with HS-142-1 (10^{-5} M), an antagonist of the natriuretic peptide guanylyl cyclase linked receptors. (cpm/well)

	Control	ET-1	ET-1 + HS	AII	AII + HS
Baseline	190 ± 24	1362 ± 288§		929 ± 186§	
ANP		420 ± 133*	630 ± 278†	161 ± 33*	882 ± 251†
BNP		240 ± 61*	766 ± 223†	156 ± 26*	813 ± 238†
CNP		296 ± 51*	1233 ± 589†	153 ± 30*	592 ± 200†

§p < 0.05 vs control; *p < 0.05 vs baseline; †p < 0.05 vs ET and AII.

These data suggest: (1) ET-1 and AII are potent stimulators for human coronary vascular smooth muscle cells proliferation. (2) ANP, BNP and CNP are potent inhibitors for ET and AII mediated human coronary smooth muscle cell proliferation. (3) These inhibitory actions of ANP, BNP and CNP are mediated by guanylyl cyclase linked natriuretic peptide receptors.

953-90 Interaction of Endothelin-1 With Vasodilators: Effects on Myocardial Contractility and Myocardial Energy Metabolism

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In contrast to in vitro experiments, which demonstrated a positive inotropy of endothelin-1 (ET-1), in vivo studies could not detect such a positive inotropy. It was supposed that the direct positive inotropy of ET-1 is counterbalanced in vivo by an indirect cardio-depressant effect due to its vasoconstrictive effect with consequent myocardial ischemia. If this hypothesis is true the positive inotropy of ET-1 should be unmasked by coronary vasodilating drugs.

We examined in open-chest rats whether adenosine (ADO: 2.0 mg/kg/min) or molsidomine (MOL: 5.0 mg/kg) can unmask this positive inotropy of 1.0 nmol/kg ET-1 i. v. by preventing myocardial ischemia. Besides measurements in the intact circulation isovolumic measurements (isovol. LVSP, isovol. dP/dt_{max}) were performed for quantification of myocardial contractility. Additionally myocardial high-energy phosphates were determined (energy charge = [ATP + 1/2ADP]/[ATP + ADP + AMP] as index of ischemia).

	ET-1	ADO + ET-1	MOL + ET-1	NaCl
Isovol. LVSP [%]	104 ± 2	113 ± 2*	108 ± 2*	97 ± 2
Isovol. dP/dt_{max} [%]	98 ± 3	120 ± 3*	115 ± 5*	100 ± 2
TPR [%]	286 ± 21*	236 ± 27*	269 ± 27*	96 ± 3
ATP [μmol/gww]	3.4 ± 0.1*	3.8 ± 0.1	4.3 ± 0.3	4.1 ± 0.1
Energy charge [%]	73 ± 3*	85 ± 2	80 ± 2	84 ± 2

Means ± SEM; hemodynamics in % of preinfusion values, *p < 0.01.

Conclusions: Adenosine and molsidomine antagonize the ET-induced vasoconstriction in part and can unmask the positive inotropy of ET-1 by preventing ET-induced myocardial ischemia.

953-91 Sustained Tissue Nitric Oxide Release After Local Delivery of a Novel Nitric Oxide Donor

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Nitric oxide (NO) is a potent vasodilator and platelet inhibitor. The local delivery of small-molecular weight NO-donors has been associated with marked biologic effects extending beyond the short half-life of these compounds. To examine the NO elaborated by vessels exposed to local delivery of NO-donors, we administered a spontaneous NO-donating compound, Dansylpiperazine nonoate (GLO/NO) (1–2 mM) intraluminally to de-endothelialized porcine carotid arteries *ex-vivo*, rinsed the vessel free of the agent, and assayed for nitrite production fluorometrically two hours after local delivery. Nitrite in the supernatant after local delivery of GLO/NO was elevated (771 ± 133 nM/gm tissue) compared to de-endothelialized control (438 ± 68; p = 0.002) and to local delivery of the vehicle (385 ± 34; p = 0.008). GLO/NO treated vessels exhibited marked displaceable NO elaboration after exposure to $HgCl_2$, compared to vehicle (920 ± 148 vs. 370 ± 69; p = 0.001) demonstrating substantial tissue thiol nitrosation by this agent.

Conclusion: Local administration of low molecular weight NO-donors results in marked NO elaboration after treatment. These observations suggest tissue bound NO promotes the prolonged biologic effects after local delivery of NO-donors and suggests a potential therapy to mitigate adverse events after vascular injury.